REMARKS

Claims 1-32 are pending in the present application. Claims 18-32 are currently under examination. Claim 18 has been amended and new Claims 33-37 have been added as indicated above. Support for amendments to the claims can be found throughout the application as filed. More particularly, support can be found, *inter alia*, at paragraphs [0005], [0038], [0039], [0063], and Examples 1, 2, 4, and 7. No new matter is added by the present amendments. Applicants respectfully submit that the remarks below place the pending claims in condition for allowance.

Rejections under 35 U.S.C. § 102(b)

Claims 18, 25, 27-28, 30 and 32

Claims 18, 25, 27-28, 30 and 32 have been rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Tang *et al.* (*NAR* Supp. 1, 2001; pages 165-66).

To be anticipatory under 35 U.S.C. § 102, a reference must teach each and every element of the claimed invention. *See Hybritech Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1379 (Fed. Cir. 1986). "Invalidity for anticipation requires that all of the elements and limitations of the claim are found within a single prior art reference … There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention." *See Scripps Clinic & Research Foundation v. Genentech, Inc.*, 927 F.2d 1565 (Fed. Cir. 1991). As discussed below, the claims of the present application are not anticipated by the cited reference, because Tang *et al.* does not teach each and every element of the rejected claims.

Tang *et al.* discloses a SNP genotyping assay using amphiphilic copolymers "consisting of oligodeoxyribonucletide … as the hydrophilic part and thermo-responsive poly(N-isopropylacrylamide) … as the hydrophobic part…." Tang *et al.*, Abstract. On average, 34 of these conjugate molecules combine to form a "colloidal nanoparticle" when heated over a phase transition temperature. *See* Tang *et al.*, p. 166. As such, Tang *et al.* teaches "colloidal nanoparticles" that each consist of a cluster of about 34 polymer-DNA conjugates.

In contrast, amended Claim 18 recites "a suspension of colloidal particles, wherein each colloidal particle comprises a single central particle associated with more than one copy of a ligand specific for said analyte…," and Claim 28 recites "a suspension of colloidal particles,

wherein said particles are coated with a lipid layer." Tang *et al.* does not teach colloidal particles that each comprise a single central particle, nor does Tang *et al.* teach a colloidal particle with a lipid layer. In contrast, Tang *et al.* teaches "colloidal nanoparticles" that each consist of a cluster of about 34 polymer-DNA conjugates.

To be anticipatory, there must be no difference between the claimed invention and the reference disclosure. *Id.* Because the Tang *et al.* reference fails to disclose colloidal particles that each comprise a single central particle or colloidal particles coated with a lipid layer, the Tang *et al.* reference fails to teach each and every limitation of Claims 18, 28, or the claims depending therefrom (including rejected Claims 25, 27, 30, and 32). Further, the Tang *et al.* reference fails to suggest any "colloidal nanoparticle" other than a cluster of polymer-DNA conjugates. Applicants therefore respectfully request withdrawal of the rejection under 35 U.S.C. § 102(b) and allowance of the pending claims.

Rejections under 35 U.S.C. § 103(a)

To establish *prima facie* obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art. *In re Royka*, 490 F.2d 981 (CCPA 1974). Obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. *In re Rinehart,* 531 F.2d 1048, 1051 (CCPA, 1976). The PTO bears the burden of establishing a case of *prima facie* obviousness. See *In re Fine*, 837 F.2d 1071, 1074 (Fed Cir. 1988). Applicants respectfully assert that a *prima facie* obviousness has not been shown because the cited references, in combination with the knowledge of one of skill in the art, do not teach or suggest all of the claim limitations.

As discussed above, Applicants' independent claims, as amended, are directed to "a suspension of colloidal particles, wherein each colloidal particle comprises a single central particle associated with more than one copy of a ligand specific for said analyte..." or " a suspension of colloidal particles, wherein said particles are coated with a lipid layer." Claims 18 and 28. The Tang *et al.* reference, in combination with the knowledge of one of skill in the art, therefore fails to teach or suggest all of the claim limitations in the independent (and therefore

dependent) claims. Further, as discussed below, it would not have been obvious to modify the assay of Tang *et al.* to arrive at the assays of the present application.

Claims 19-21 and 30

Dependent Claims 19-21 and 30 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tang *et al.* in view of Singh *et al.* (U.S. Patent Publication No. 20020034827). Singh *et al.* discloses general methods and materials for the extraction and analysis of complex materials. *See* Singh *et al.*, Abstract.

Claim 19 recites "a first population and a second population of colloidal particles," while Claim 20 recites larger colloidal particles in the first population. Claim 21 recites different labeling in the first and second population, while Claim 30 recites a means for detecting comprising a fluorescence detector.

Although Tang *et al.* does not disclose more than one population of colloidal particles, the Examiner asserts that it would have been obvious for a skilled artisan to use at least two populations of nanoparticles in the assay of Tang *et al.* with a reasonable expectation of success. Office Action, at pp. 4-5. However, this assertion reflects a failure to recognize that the "colloidal nanoparticles" of Tang *et al.* each consist of a cluster of polymer-DNA conjugates. Because the "colloidal nanoparticles" of Tang *et al.* exist only when these clusters form, one of skill in the art would not have known how to modify the clusters of Tang *et al.* to achieve a colloidal particle with a single central particle. Further, one of skill in the art would not have known how more than one population of these clusters would interact, particularly if these particles were to co-exist with a lipid layer. One of skill in the art would also not have known how to use the light transmittance method of Tang *et al.* to differentiate a phase transition for at least two populations of such clusters. The Singh *et al.* reference discloses only general concepts regarding the extraction and analysis of complex materials and provides no guidance to address any of these issues.

As such, Tang *et al.* fails to teach or suggest all of the claim limitations of Claims 19-21 and 30 in view of Singh *et al.* Further, one of skill in the art would not have been motivated to combine the Tang *et al.* and Singh *et al.* references to arrive at the assays of Claim 19-21 and 30,

nor would one of skill in the art have arrived at the assays with a reasonable expectation of success.

Claims 22-24 and 31

Dependent Claims 22-24 and 31 have been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tang *et al.* in view of Schaertl *et al.* (*J Biomol Screen* 2000; 5(4):227-237). Schaertl *et al.* discloses the labeling of nanoparticles for immunoassays. *See* Schaertl *et al.*, Abstract.

Claim 22 recites a lipid layer, while Claims 23 and 31 recite a natural cell membrane. Claim 24 recites covalent linking between the ligand and colloidal particle.

Although Tang *et al.* does not disclose a lipid layer, the Examiner asserts that the nanoparticle of Schaertl *et al.* inherently includes a lipid layer and could be used to increase the range of analytes for detection in Tang *et al.* However, the Tang *et al.* reference focuses solely on SNP genotyping, failing to teach or suggest any other method of analyte detection. Even if one of skill in the art were to know that Schaertl *et al.* discloses nanoparticles that inherently have a lipid layer, one of skill in the art would not have known how such a lipid layer would aid in detecting hybridization of the polymer-DNA conjugates with complementary DNA particles taught in Tang *et al.* Further, because the "colloidal nanoparticles" of Tang *et al.* each consist of a cluster of polymer-DNA conjugates, one of skill in the art would not have known how such a lipid layer would affect the interaction and detection of polymer-DNA conjugates, much less colloidal particle comprising a single central particle or a lipid layer.

As such, Tang *et al.* fails to teach or suggest all of the claim limitations of Claims 22-24 and 31 in view of Schaertl *et al.* Further, one of skill in the art would not have been motivated to combine the Tang *et al.* and Schaertl *et al.* references to arrive at the assays of Claim 22-24 and 31, nor would one of skill in the art have arrived at the assays with a reasonable expectation of success.

Claim 26

Dependent Claim 26 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tang *et al.*

Claim 18 recites an assay for detecting the binding of an analyte to a ligand by determining transition from a first to a second phase, while Claim 26 recites that the first phase is a condensed phase and second phase is a dispersed phase.

Tang *et al.* discloses the aggregation of "colloidal nanoparticles" upon DNA hybridization. *See* Tang *et al.*, at p. 166. However, Tang *et al.* does not disclose the dispersion of "colloidal nanoparticles" upon DNA hybridization, nor does Tang *et al.* disclose the dispersion of any other type of particle. Further, because the "colloidal nanoparticles" of Tang *et al.* each consist of a cluster of polymer-DNA conjugates, one of skill in the art would not have known whether particles in the Tang *et al.* assay would disperse, which particles would disperse (*i.e.*, the "colloidal nanoparticles" themselves or clusters of "colloidal nanoparticles"), or how dispersion would occur given the fact that the properties of the polymer-DNA conjugates in the Tang *et al.* assay allow for the formation of "colloidal nanoparticles" and aggregation of clusters.

As such, Tang *et al.* fails to teach or suggest all of the claim limitations of Claim 26. Further, one of skill in the art would not have been motivated to modify the assay of Tang *et al.* to arrive at the assay of Claim 26, nor would one of skill in the art have arrived at the assays with a reasonable expectation of success.

Claim 29

Finally, dependent Claim 29 has been rejected under 35 U.S.C. § 103(a) as allegedly being unpatentable over Tang *et al.* in view of Faulds *et al.* (*Analyst* 2002; 127:282-86). Faulds *et al.* discloses the use of a microscope to detect light scattering of gold or silver colloid surfaces. Faulds *et al.*, Abstract.

Claim 29 recites detection using a microscope.

As discussed above, the Tang *et al.* reference, in combination with the knowledge of one of skill in the art, does not teach or suggest all of the claim limitations of Claim 28 or the claims depending therefrom (including Claim 29). Further, Tang *et al.* actually distinguishes their "colloidal nanoparticles" over DNA-linked colloidal gold nanoparticles like those detected using a microscope in Faulds *et al.* *See* Tang *et al.*, at p. 165.

As such, Tang *et al.* fails to teach or suggest all of the claim limitations of Claim 29. Further, because the Tang et al. reference actually teaches away from detecting a particle like

those taught in Faulds *et al.*, one of skill in the art would not have been motivated to combine the Tang *et al.* reference and Faulds *et al.* references to arrive at the assay of Claim 29.

New Claims 33-37

New Claims 33-37 depend from Claim 18 or 28 and characterize the single central particle.

As discussed above, the Tang *et al.* reference does not teach or suggest a single central particle associated with more than one copy of a ligand specific for an analyte, much less a single central particle that comprises silica or a metal. In fact, as discussed above, Tang *et al.* distinguishes their "colloidal nanoparticles" from such particles (*e.g.*, DNA-linked colloidal gold nanoparticles). *See* Tang *et al.*, at p. 165.

As such, Tang *et al.* fails to teach or suggest all of the claim limitations of new Claims 33-37. Further, one of skill in the art would not have been motivated to modify the Tang *et al.* assay to arrive at the assays of new Claims 33-37.

The Tang *et al.* reference, in combination with the knowledge of one of skill in the art and the cited references, does ***not*** teach or suggest all of the claim limitations, nor would it have been obvious to modify the assay of Tang *et al.* to arrive at the claimed methods. Applicants therefore respectfully request withdrawal of the rejections under 35 U.S.C. § 103(a).

Conclusion

For the foregoing reasons, it is respectfully submitted that the rejections set forth in the outstanding Office Action have been addressed and that the application is in condition for allowance. Accordingly, Applicants request the expeditious allowance of the pending claims.

The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to call the undersigned attorney to resolve such issues promptly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

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